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## Prophylactic fasciotomy in a porcine model of extremity trauma



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### ABSTRACT

**Background:** Extremity injury, with concomitant hemorrhagic shock, can result in ischemia–reperfusion injury and the formation of compartment syndrome requiring fasciotomy. As the benefit of prophylactic fasciotomy is unclear, the objective of this study is to determine the functional recovery of an ischemic limb with hemorrhagic shock after prophylactic fasciotomy.

**Material and methods:** Yorkshire swine underwent 35% blood volume hemorrhage, followed by 1, 3, and 6 h of ischemia ( $n = 17$ ; 1HR, 3HR, and 6HR) via iliac artery occlusion followed by repair and reperfusion. A second cohort ( $n = 18$ ) underwent fasciotomy of the anterior compartment of the hind limb following vascular repair (1HR-F, 3HR-F, and 6HR-F). Compartment pressures, measures of electromyographic (EMG) recovery, and a validated gait score (modified Tarlov) were performed throughout a 14-d survival period.

**Results:** Increasing ischemic intervals resulted in incremental increases in compartment pressure ( $P < 0.05$ ), although the mean did not exceed 30 mm Hg. EMG studies did not show a significant improvement comparing the 3HR with 6HR groups. There was a significant improvement in the EMG studies within the 3HR-F, when compared with 6HR-F. There was a trend toward sensory improvement between the 3HR-F and 3HR groups. However, this did not translate to a difference in functional outcome as measured by the Tarlov gait score.

**Conclusions:** Within this swine model of hemorrhagic shock and hind limb ischemia, the use of prophylactic fasciotomies did not improve functional outcome.

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## 1. Introduction

Extremity vascular trauma represents 75%–88% of vascular injury in the wars in Iraq and Afghanistan [1–3], with limb salvage attempted in almost 80% of patients [4,5]. This is higher than in previous conflicts, largely due to a reduction in prehospital transport time and the availability of adjuncts, such as temporary vascular shunts, which can increase the physiological window for limb salvage [6].

Limb salvage is dependent on the early restoration of arterial inflow and venous outflow in addition to the mitigation of reperfusion injury [7]. A local effect of reperfusion injury is tissue edema driven by the inflammatory process initiated by ischemic insult. If the resultant increase in compartment pressure exceeds the capillary pressure, limb viability can become compromised, a pathology known as compartment syndrome [8,9]. Although compartment syndrome is a clinical diagnosis and there is no standard quantitative definition, an absolute pressure >30 mm Hg is considered a risk factor for compartment syndrome [10]. The clinical standard of practice for ameliorating extremity compartment syndrome is fasciotomy.

Although the benefit of fasciotomies in clinically established compartment syndrome is unquestioned, prophylactic use following emergent revascularization is less clear [10,11]. The use of fasciotomy in limb salvage has the potential to maximize functional outcome; however, fasciotomies are not without morbidity and can result in significant reconstructive soft tissue complications [12]. Specifically, what is unclear is the optimal ischemic time and compartment pressure threshold for fasciotomy to achieve maximal benefit in functional outcome.

The purpose of this study was to evaluate the effect of prophylactic fasciotomy on neuromuscular recovery, laboratory markers of ischemia–reperfusion, and tissue injury as determined by histologic evaluation. We hypothesized that prophylactic fasciotomy would facilitate the preservation of limb function and improve neuromuscular recovery when compared with a treatment modality that did not include fasciotomy.

## 2. Methods

Institutional Animal Care and Use protocol review and approval was obtained for the study. All studies were performed at the accredited laboratories of the United States Army Institute of Surgical Research at Fort Sam Houston, TX. This study used female Yorkshire swine of weights ranging from 70–90 kg (*Sus scrofa*; Midwest Research Swine, Gibbon, MN). On arrival, swine were housed for 7 d before their use in experimental protocols for quarantine and acclimation.

### 2.1. Study design

On the day of surgery, swine were randomized into one of six experimental groups as follows: vascular injury—1, 3, or 6 h of ischemia without fasciotomy (1HR, 3HR, and 6HR) or vascular injury—1, 3, or 6 h of ischemia with prophylactic fasciotomy

(1HR-F, 3HR-F, and 6HR-F). The study was executed in five phases as described in the following and outlined in Figure 1.

### 2.2. Preparation

Induction of anesthesia was achieved with an intramuscular (IM) injection of ketamine (15–20 mg/kg IM), atropine (0.04–0.4 mg/kg IM), and surgical plane of anesthesia maintained with 2%–4% isoflurane following orotracheal intubation. All surgical procedures were performed using sterile precautions with the animal in the supine position. A fentanyl patch (25 mcg/hr) was placed before surgery to ensure effective postoperative pain control.

Using a midline cervical incision, the right common carotid and internal jugular vein were cannulated to permit intravenous fluid resuscitation and arterial pressure monitoring. A lower abdominal midline incision was performed to expose the right external iliac artery via dissection of the preperitoneal plane. A 5–6-cm segment of the vessel was exposed using the bifurcation of the femoral arteries serving as the distal landmark. The lateral circumflex artery was also identified and ligated to reduce the collateral arterial extremity inflow. Silastic vessel loops were used to gain hemostatic control, and the right external iliac artery cannulated with an 8 Fr catheter for the purpose of simultaneously achieving controlled hemorrhage and inducing vascular extremity injury and ischemia.

### 2.3. Hemorrhage, shock, and resuscitation

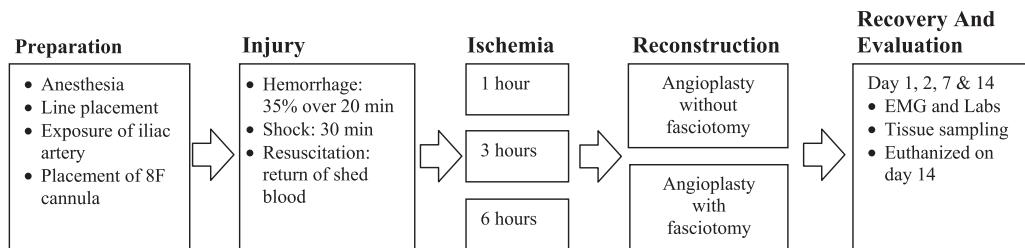
Hemorrhagic shock was induced using a previously described and accepted methodology [13]; briefly, 35% of swine total blood volume was withdrawn through the iliac catheter over 20 min with half of that volume withdrawn over the first 7 min and the remaining volume of the next 13 min. Control and accuracy of volume withdrawal was ensured by the use of a computer-driven rotary pump (Masterflex Easy Load II; Cole–Parmer, Vernon Hills, IL). The animals then remained in untreated hypovolemic shock for 30 min. At the completion of the shock period, maintenance intravenous fluid (normal saline at 150 cc/h) was started. Animals were resuscitated using autologous fresh whole blood collected during the controlled hemorrhage phase and normal saline boluses (500 cc) to achieve and maintain a mean arterial pressure of ≥60 mm Hg.

### 2.4. Ischemic interval

Subsequent to the shock interval and restoration of blood pressure, animals were randomized into the previously described six experimental groups. Limb ischemia was achieved by clamping the external iliac artery, abolishing distal flow, which was confirmed by Doppler.

### 2.5. Arterial reconstruction and fasciotomy

After the assigned ischemic interval, restoration of blood flow to the hind limb was achieved by performing a patch angioplasty. The resultant puncture wound from the cannula removal was extended proximally and distally for an incision

**Fig. 1 – The five phases of the study protocol.**

size of approximately 2–4 cm. Inflow and outflow were assessed and if satisfactory, the artery was flushed proximally and distally with dilute heparin (10 U/mL). If flow was unsatisfactory, a thrombectomy was performed using a 3 Fr Fogarty catheter (Edward Lifesciences, Irving, CA) until flow was restored. The angioplasty was fashioned from Dacron Patch sutured with 6'0 Prolene. Confirmation of flow through the completed patch was accomplished by Doppler. If the arterial flow was occluded beneath the patch at the time of operative repair, the patch was removed, thrombectomy performed, and the angioplasty repeated.

In animals assigned to the fasciotomy group, a fasciotomy of the anterior compartment was performed at the time of flow restoration. An 8–10 cm longitudinal incision was made over the anterior compartment exposing the fascia. After opening the fascial compartment, the muscle belly was detached from the bone to ensure adequate compartment release. A Jacobs Ladder was then created with packing of two 4 × 4 pieces of moist gauze in the open wound.

At the conclusion of the reconstruction and fasciotomy phase, the abdominal and neck incisions were closed in layers with staples to the skin. On postoperative day 1, the fasciotomy site was irrigated and scrubbed with a Hibiclenz (Mölnlycke Health Care, Norcross, GA) and the skin closed with 2'0 Prolene in a vertical mattress configuration.

## 2.6. Recovery

Postoperatively, animals were permitted to eat, drink, and interact normally. Analgesia was provided by the fentanyl patch (25 mcg/hr) placed before surgery and breakthrough analgesia of buprenorphine (0.01–0.05 mg/kg) was administered by the veterinarian *pro re nata*. Aspirin (81 mg/d) and Rocephin (2 g/day) were administered on a daily basis.

## 2.7. Primary study end points

Primary end points for this study included compartment pressure, electromyographic (EMG) studies, and a validated porcine gait score (modified Tarlov scale) [14]. All points were measured as a baseline, postoperatively, and on day 1, 2, 7, and 14.

Anterior compartment pressures were evaluated using a Stryker Intra-Compartmental Pressure Monitor (Stryker, Kalamazoo, MI) and consisted of an average of three sequential readings in the anterior compartment containing the peroneus muscle of the hind limb. Preoperative compartment pressures were measured after the induction of anesthesia.

Postoperatively, in animals with an open fasciotomy, the reading was obtained from the exposed muscle belly. On postoperative day 1, the compartment pressure was determined after closure of the wound.

EMG studies were used as an indirect method to evaluate limb function. Compound motor action potentials (CMAP) were obtained by stimulation of the peroneal nerve with external sensors placed over the anterior compartment muscle belly and knee. Sensory nerve action potential (SNAP) was collected by stimulation of the mixed tibial nerve at the foot with subcutaneous needles placed at fixed distances. Nerve conduction velocities (NCV) were calculated via CMAP waveform. Each nerve conduction study was reproduced three times by a single user. Spot checks of waveforms were performed by a board-certified neurologist.

Gait assessment was performed daily for the duration of the study using the modified Tarlov scale, which consists of an ordinal scale 0–4 (Table 1). Animals score 0 if they have an insensate paralyzed limb and 4 if they demonstrate no gait abnormality.

## 2.8. Secondary end points

Secondary end points consisted of laboratory indices of reperfusion injury and muscle and nerve tissue damage as determined by histopathologic evaluation. Laboratory indices consisted of K<sup>+</sup>, lactate, creatinine phosphokinase (CK), myoglobin, and lactate dehydrogenase. All laboratory analyses were performed using arterial blood sampled from either the right internal carotid artery or a superficial arterial sample from the hind limb.

Duplex ultrasound was performed on the anesthetized animals during the routine postoperative follow up.

On postoperative day 14, while under general anesthesia, primary and secondary end points were evaluated. Tissue harvest of the peroneus muscle and nerve occurred before

**Table 1 – Modified Tarlov gait scale.**

Scale	Description
0	Insensate, paralyzed limb.
1	Able to sit.
2	Stands but unable to bear weight on affected limb.
3	Stands and walks but with gait or posture abnormality.
4	No gait or posture abnormality.

**Table 2 – Pathologic grading system.**

Score	Peroneus tertius muscle	Peroneal nerve degeneration	Peroneal nerve inflammation
0	No involvement	No involvement	No involvement
1	1%–25% cross-sectional area	Mild	Minimal
2	26%–50% cross-sectional area	Moderate	Mild
3	51%–75% cross-sectional area	Severe	Moderate
4	76%–100% cross-sectional area		Severe

euthanization. Samples were placed in formalin, stained with hematoxylin and eosin, and Masson trichrome, which was scored by a veterinary pathologist for degeneration and inflammation (Table 2).

## 2.9. Statistical analysis

Statistical analysis was completed using SAS 9.2 Software (SAS Institute, Cary, NC). Data are reported as mean and standard error unless otherwise specified. One way analysis of variance was used to calculate a difference among means for quantitative measures. Post hoc t-tests were performed if the analysis of variance identified a significant difference among groups. Wilcoxon–Mann tests were used for comparison of histopathologic data. Results are considered significant when  $P \leq 0.05$ .

## 3. Results

The study comprised the following six study groups (as described in the methods): 1HR  $n = 6$ , 3HR  $n = 5$ , 6HR  $n = 6$ , 1HR-F  $n = 6$ , 3HR-F  $n = 6$ , and 6HR-F  $n = 6$ . Five animals expired within the first 24 h and were replaced, with necropsy identifying cardiopulmonary failure secondary to disseminated intravascular coagulopathy as the cause of death (3HR = 3,

3HR-F = 2). These animals were excluded from the analysis. There was no statistically significant difference in the animal baseline characteristics among groups (Table 3).

## 3.1. Primary end points

### 3.1.1. Compartment pressure measurements

In the no fasciotomy group, the highest mean compartment pressure measurements (CPMs) in each group was  $10.1 \pm 1.7$  for 1HR on day 1,  $15.3 \pm 1.4$  for 3HR on day 7, and  $27.4 \pm 3.6$  for 6HR on day 1. When performing comparisons by time point (Fig. 2), at 6 h there was a significant increase in CPMs in the 3HR and 6HR groups with respect to the 1HR group. Post-operatively and on days 1, 2, and 7, the 6HR group had significantly greater CPMs when compared with the 1HR and 3HR groups. There was no difference in CPMs across the groups on day 14.

Within the fasciotomy group, the highest mean CPM in each group occurred on day 1 and were  $10.0 \pm 1.3$  for 1HR-F,  $10.3 \pm 2.4$  for 3HR-F, and  $15.1 \pm 2.3$  for 6HR-F. There was no significant difference detected when comparing CPM readings by time point (Fig. 2).

Intergroup comparisons among the 3HR and 3HR-F ( $15.3 \pm 1.3$  versus  $7.2 \pm 1.7$ ,  $P < 0.05$ ) groups had a statistically significant difference on Day 7. Comparing 6HR and 6HR-F a

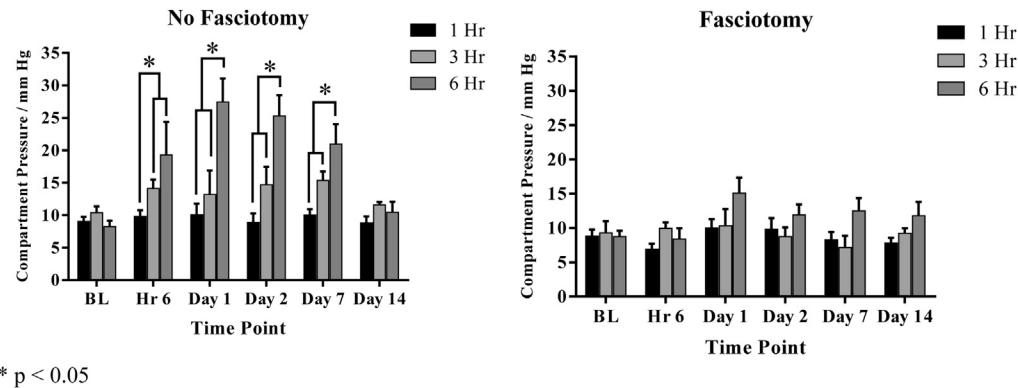
**Table 3 – Baseline characteristics.**

Variable, mean $\pm$ SE	1 HR, n = 6	1HR-F, n = 6	3HR, n = 5	3HR-F, n = 6	6HR, n = 6	6HR-F, n = 6	P
Weight, kg	$76.5 \pm 1.2$	$73.7 \pm 3.6$	$76.2 \pm 1.5$	$76.6 \pm 2.6$	$73.8 \pm 2.9$	$77.9 \pm 1.7$	0.783
MAP, mm Hg	$72 \pm 2.6$	$60 \pm 4.3$	$70 \pm 8.3$	$66 \pm 4.2$	$54 \pm 6.2$	$63 \pm 7.3$	0.278
Vascular							
Fem a velocity, cm/s	$54.3 \pm 3.2$	$63.2 \pm 5.3$	$49.1 \pm 4.2$	$55.9 \pm 6.2$	$56.0 \pm 7.7$	$58.8 \pm 5.5$	0.660
Compartment press, mm Hg	$9.0 \pm 0.7$	$8.8 \pm 1.0$	$10.4 \pm 1.0$	$9.2 \pm 1.7$	$8.2 \pm 1.0$	$8.7 \pm 0.9$	0.822
Nerve conduction studies							
CMAP, mV	$12.5 \pm 0.9$	$9.3 \pm 0.7$	$13.3 \pm 1.7$	$10.2 \pm 0.9$	$12.3 \pm 0.9$	$9.8 \pm 1.3$	0.069
SNAP, uV	$14.5 \pm 1.6$	$13.3 \pm 1.2$	$13.4 \pm 1.6$	$14.9 \pm 1.4$	$12.4 \pm 0.7$	$11.0 \pm 1.4$	0.344
NCV, m/s	$57.8 \pm 2.7$	$56.4 \pm 3.0$	$58.1 \pm 3.2$	$56.8 \pm 3.0$	$60.7 \pm 2.9$	$55.4 \pm 3.0$	0.858
Laboratory							
Hb, g/dL	$10.2 \pm 0.4$	$10 \pm 0.4$	$9.6 \pm 0.5$	$9.7 \pm 0.3$	$9.4 \pm 0.3$	$9.8 \pm 0.3$	0.685
K <sup>+</sup> , mEq/L	$3.9 \pm 0.1$	$4.0 \pm 0.1$	$4.3 \pm 0.5$	$3.9 \pm 0.1$	$3.8 \pm 0.1$	$4.1 \pm 0.2$	0.605
Lactate, U/L	$1.1 \pm 0.3$	$1.3 \pm 0.1$	$1.7 \pm 0.5$	$1.3 \pm 0.2$	$1.2 \pm 0.3$	$1.7 \pm 0.3$	0.500
CK, ug/L	$1548 \pm 918$	$807 \pm 163$	$1272 \pm 431$	$636 \pm 67$	$1009 \pm 266$	$688 \pm 74$	0.508
Myoglobin, ng/mL	$47 \pm 11.3$	$49.3 \pm 14.9$	$38 \pm 7.6$	$40 \pm 7.2$	$26 \pm 2.1$	$46 \pm 7.7$	0.408
LDH, U/L	$298 \pm 70$	$301 \pm 58$	$341 \pm 33$	$275 \pm 28$	$228 \pm 40$	$248 \pm 35$	0.493

CK = creatinine phosphokinase; compartment press = compartment pressure; fem a velocity = common femoral artery velocity; Hb = hemoglobin; K<sup>+</sup> = potassium; LDH = lactate dehydrogenase; MAP = mean arterial pressure; SE = standard error.

No statistical difference among groups was identified.

P < 0.05 is the statistical significance across all groups.



**Fig. 2 – Anterior compartment pressure results for animals with no fasciotomy and fasciotomy for 1, 3, and 6 h duration of ischemia. In the no fasciotomy group, animals undergoing 6 h of ischemia had significantly higher pressures compared with 1 and 3 h groups. There was no difference in pressures across the fasciotomy groups \*P < 0.05.**

statistical difference was found from the postoperative period through Day 7.

### 3.1.2. EMG studies

CMAP, SNAP, and NCV were measured on the scheduled postoperative days. On postoperative day 14, within the no fasciotomy group, the CMAP value (millivolt) in the 1HR group was significantly higher than either the 3HR or 6HR groups, where the latter two groups were not found to be significantly different ( $10.3 \pm 1.0$  versus  $5.9 \pm 1.5$  and  $3.2 \pm 1.4$ , respectively;  $P < 0.05$ ). This trend was reversed in the fasciotomy group, when the 1HR-F and 3HR-F CMAP values were similar to each other but significantly higher than the 6HR-F group ( $4.5 \pm 0.3$  versus  $4.9 \pm 1.3$  and  $1.6 \pm 0.7$ , respectively;  $P < 0.05$ ) (Fig. 3). Comparing the groups at the ischemic intervals, there was a worse recovery of the 1HR-F and 1HR ( $10.3 \pm 1.0$  versus  $4.5 \pm 0.3$ ;  $P < 0.05$ ).

This pattern was also observed with the SNAP readings (Fig. 4). The reading (millivolt) from the 1HR group in the no fasciotomy cohort was higher than the 3HR and 6HR groups ( $14.9 \pm 2.1$  versus  $8.1 \pm 1.5$  and  $5.0 \pm 0.9$ , respectively;  $P < 0.05$ ). In the fasciotomy group, both the 1HR-F and 3HR-F groups had significantly higher values than the 6HR group ( $11.5 \pm 1.1$  versus  $11.3 \pm 1.1$  and  $5.1 \pm 1.4$ , respectively;  $P < 0.05$ ). No difference was found comparing the fasciotomy and no fasciotomy group at the given ischemic intervals.

NCV were not found to be statistically significantly different.

### 3.1.3. Tarlov gait scale

The lowest scores all occurred on the first postoperative day. Within the fasciotomy group, the mean scores per 1, 3, and 6 h groups were  $1.2 \pm 0.7$ ,  $1.0 \pm 0.5$ , and  $0.5 \pm 0.2$ , respectively. This observation was found to be similar in the fasciotomy groups, which had mean scores per 1, 3, and 6 h groups of  $1.7 \pm 0.5$ ,  $1.3 \pm 0.7$ , and  $0.3 \pm 0.2$ , respectively. All groups demonstrated a sequential improvement in their scores over the 14 postoperative days with no significant difference within groups detected at any time point (Fig. 5). The scores for the no fasciotomy group at day 14 per 1, 3, and 6 h groups were  $3.7 \pm 0.3$ ,  $3.4 \pm 0.6$ , and  $3.6 \pm 0.2$ , respectively. Within the fasciotomy group, the scores were  $4.0 \pm 0.0$ ,  $3.8 \pm 0.2$ , and  $3.2 \pm 0.4$ , respectively.

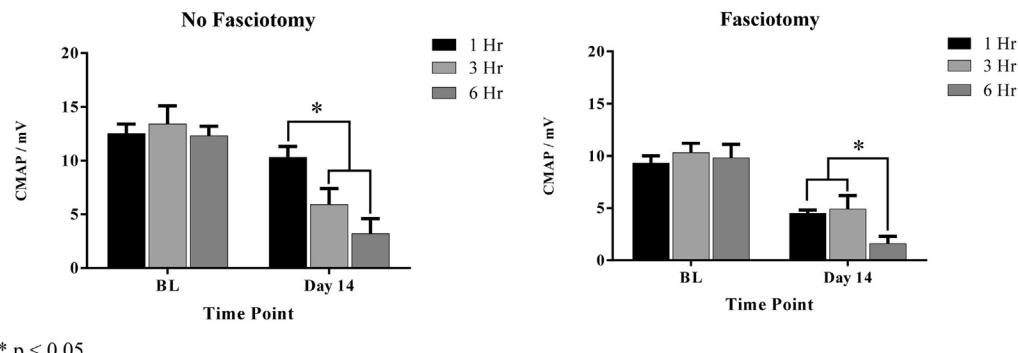
## 3.2. Secondary end points

### 3.2.1. Laboratory indices of reperfusion

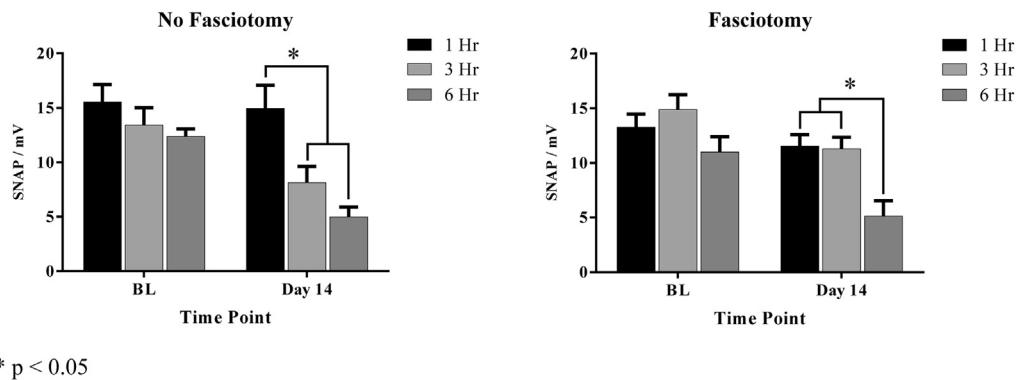
There was no difference, by time point, between groups within the no fasciotomy and fasciotomy groups for the measured ischemic markers (Table 4).

### 3.2.2. Duplex ultrasound

Mean femoral artery velocities on day 14 were significantly reduced in the 3HR-F group when compared with their



**Fig. 3 – CMAP values for animals with no fasciotomy and fasciotomy for 1, 3, and 6 h duration of ischemia. In the no fasciotomy group, the 3 and 6 h groups had significantly lower CMAP values than the 1 h group. In the fasciotomy group, animals undergoing 1 and 3 h of ischemia had higher CMAP values than those undergoing 6 h \*P < 0.05.**



**Fig. 4 – SNAP values for animals with no fasciotomy and fasciotomy for 1, 3, and 6 h duration of ischemia. In the no fasciotomy group, the 3 and 6 h groups had significantly lower SNAP values than the 1 h group. In the fasciotomy group, animals undergoing 1 and 3 h of ischemia had higher SNAP values than those undergoing 6 h \*P < 0.05.**

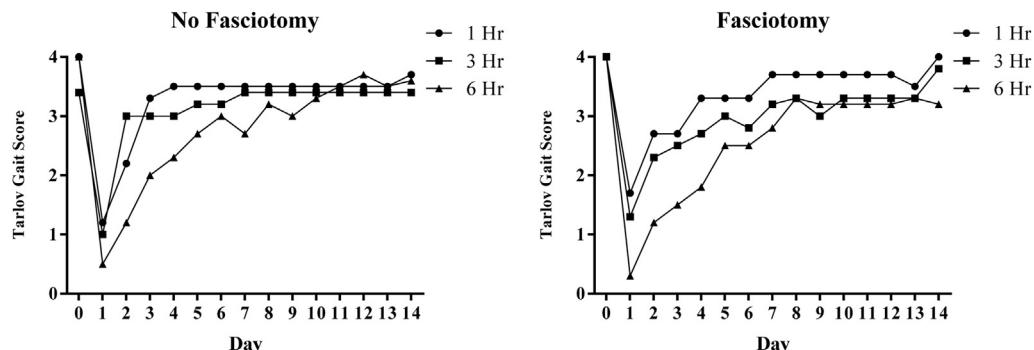
respective baseline ( $55.9 \pm 15.3$  versus  $44.5 \pm 19.0$ ;  $P = 0.02$ ). There was a significantly decreased flow in 3HR-F compared with 3HR ( $44.5 \pm 7.8$ ,  $68.3 \pm 6.3$ ;  $P = 0.041$ ). No other significant differences were found on postoperative day 14.

### 3.2.3. Histopathology

Differences among groups were found for nerve inflammation and muscle fibrosis (Table 5). Post hoc analysis revealed a difference between 1HR when compared with 6HR across all variables. The 1HR group had less insult with regards to nerve inflammation and muscle fibrosis compared with the 3HR. The fasciotomy groups were not found to be statistically different. 1HR-F had increased nerve and muscle damage across all variables compared with 1HR.

## 4. Discussion

This is the first study to use a clinically relevant porcine model of vascular injury, in the setting of hemorrhage, to study the changes in extremity compartment pressures, following reperfusion. This study is a continuation of our group's previous work, where concurrent Class III shock in addition to extremity ischemia has been shown to have a deleterious effect on functional outcome, maximal at 3 h of ischemia [13].



**Fig. 5 – Mean Tarlov gait scale scores for animals with no fasciotomy and fasciotomy for 1, 3, and 6 h duration of ischemia. Both groups demonstrated a sequential improvement in their scores over the 14 postoperative days with no significant difference within groups detected at any time point.**

This is particularly relevant to military surgery where extremity injury and shock constitute a significant burden of injury.

Fasciotomies help to minimize impedance to venous outflow by decompressing fascial compartments. This strategy is well established in the setting of elevated compartment pressures seen in compartment syndrome, where fasciotomy has been shown to improve functional outcome. Indeed, delayed or incomplete fasciotomies are associated with limb loss and increased mortality [15]. However, the role of prophylactic fasciotomies is unclear, which remains an important unanswered question as unnecessary fascial decompression is associated with a substantial burden of morbidity [12].

The present study demonstrated a step-wise increase in compartment pressures for 1, 3, and 6 h of ischemia, although none exceeded the current threshold definition of compartment syndrome of 30 mm Hg. The study goes on to explore the role of prophylactic fasciotomies within this model. EMG studies were suggestive of a superior neuromuscular recovery in the 3 h group with fasciotomy compared with the group without, but this did not translate to a difference in functional gait scores at 2 wk. This study suggests that prophylactic fasciotomies have a limited role in improving function outcome where compartment pressures do not exceed current threshold definitions.

**Table 4 – Day 14 results.**

Variable, mean ± SE	1 HR, n = 6	1HR-F, n = 6	3HR, n = 5	3HR-F, n = 6	6HR, n = 6	6HR-F, n = 6	P
Tarlov	3.7 ± 0.3	4 ± 0.0	3.4 ± 0.6	3.8 ± 0.2	3.6 ± 0.2	3.2 ± 0.4	0.629
Vascular							
Fem a velocity, cm/s	59.8 ± 5.1	64.2 ± 10.6	68.3 ± 6.3	44.5 ± 7.8	61.1 ± 6.8	65.1 ± 5.4	0.014
Compartment press, mm Hg	8.7 ± 1.0	7.8 ± 1.8	11.6 ± 1.0	9.2 ± 1.9	10.4 ± 3.9	11.8 ± 4.9	<0.01
Nerve conduction studies							
CMAP, mV	10.3 ± 1.0	4.5 ± 0.3	5.9 ± 1.5	4.9 ± 1.3	3.2 ± 1.4	1.6 ± 0.7	<0.01
SNAP, uV	14.9 ± 2.1	11.5 ± 1.0	8.1 ± 1.5	11.3 ± 1.1	5.0 ± 0.9	5.1 ± 1.4	<0.01
Laboratory							
Hb, g/dL	12.4 ± 0.2	10.7 ± 0.3	11.7 ± 0.6	10.7 ± 0.4	10.9 ± 0.6	10.1 ± 0.3	0.194
K <sup>+</sup> , mEq/L	3.8 ± 0.1	3.6 ± 0.1	3.8 ± 0.1	3.7 ± 0.2	3.8 ± 0.3	3.7 ± 0.2	0.143
Lactate, U/L	1.3 ± 0.2	2.5 ± 1.0	1.4 ± 0.5	2.2 ± 0.8	2.8 ± 0.9	1.9 ± 0.5	0.169
CK, ug/L	2230 ± 684	2186 ± 594	2522 ± 575	1552 ± 788	2159 ± 412	2617 ± 322	0.674
Myoglobin, ng/mL	63 ± 32	48 ± 8.7	39 ± 7.3	23 ± 6.9	39 ± 6.5	22 ± 2.2	0.458
LDH, U/L	519 ± 50.8	647 ± 99.0	727 ± 128	567 ± 122	684 ± 73.9	606 ± 97.7	0.469

CK = creatinine phosphokinase; compartment press = compartment pressure; fem a velocity = common femoral artery velocity; Hb = hemoglobin; K<sup>+</sup> = potassium; LDH = lactate dehydrogenase; MAP = mean arterial pressure; SE = standard error.  
P < 0.05 is the statistical significance across all groups.

Limitations of the current model are related to the acquisition of the Tarlov score. The blinded procedure was not performed by the same provider on a daily basis. Therefore, variability could account for the recovery of the 6-h ischemia animals when the previous published studies had a decreased functional recovery [13,14]. The Tarlov score also did not correlate with the EMG findings or histopathologic data of this study. Another limitation was with wound complications of the fasciotomy. The closure of the wounds did not result in surgical site infections but many animals developed seromas, which decreased EMG-evoked potentials due to increased resistance across the sensors and nerves. The fasciotomy animals may have had improved EMG studies.

The porcine hind limb has differences in comparison with the compartment. The leg (below the knee) had two compartments, anterior and posterior in comparison with the four compartment human leg. The posterior compartment did not have an elevation in compartment pressures on model development and was not released. The anterior compartment also contained the peroneal nerve, where the CMAP and NCV were measured, and the peroneus tertius muscle, which was histologically evaluated. The mixed tibial nerve did not course through the anterior compartment. The technique of compartment release of detaching the peroneus muscle off

the bone may have caused damage to the neurovascular bundle, again limiting the quality of EMG data and effecting of histopathology evaluation as seen in the 1HR-F group.

There are several published animal models of compartment syndrome; however, the present study is unique in its length of follow-up, function outcome measures, and the presence of concomitant shock. The majority of previous investigators have used balloon catheters or fluid infusion to induce compartment syndrome, along with histology as their main outcome [16–18].

Sheridan and Matsen [16] demonstrated a critical threshold of 50 mm Hg applied over 24 h to the anterior compartment of the rabbit using a latex balloon, to achieve irreversible necrosis. A similar methodology was used recently by Kalns et al. [17] who used inflation pressures of 30 mm Hg for 5 and 6 h in the anterior compartment of the pig. They produced sustained post-deflation compartment pressure of around 40 mm Hg for the duration of the 8 h post injury follow-up. Hargens et al. [18] used an intramuscular infusion of plasma in dogs to maintain an elevated anterior compartment pressure in groups between 20 and 120 mm Hg for 8 h and then followed up for 48 h. They concluded on the basis of the histologic appearance of necrosis that the threshold for fasciotomy should be 30 mm Hg.

**Table 5 – Pathology result for nerve and muscle histology on postoperative day 14.**

Characteristic, mean ± SE	1HR	3HR	6HR	1HR-F	3HR-F	6HR-F	P
Nerve							
Degeneration	0.67 ± 0.21	2.0 ± 0.71	1.8 ± 0.37	1.6 ± 0.22	1.67 ± 0.42	2.0 ± 0.45	0.172
Inflammation	0.17 ± 0.17	1.75 ± 0.63	1.6 ± 0.40	0.80 ± 0.18	1.67 ± 0.42	1.67 ± 0.33	0.032
Muscle							
Degeneration	0.67 ± 0.21	1.6 ± 0.60	2.83 ± 0.60	1.5 ± 0.50	1.83 ± 0.40	1.67 ± 0.33	0.060
Inflammation	0.67 ± 0.33	1.4 ± 0.75	2.67 ± 0.61	1.33 ± 0.33	1.83 ± 0.54	1.5 ± 0.50	0.235
Fibrosis	0.50 ± 0.22	1.6 ± 0.40	2.83 ± 0.48	1.33 ± 0.33	2.0 ± 0.45	1.8 ± 0.40	0.012

SE = standard error.

P < 0.05 is the statistical significance across all groups.

In terms of the application of fasciotomy to animal models, the present study extends the findings of several studies examining the role of timing of this intervention [19,20]. Rorabeck and Clarke [19] elevated the anterior compartment pressure of dogs by infusing blood to pressures between 40 and 160 mm Hg and performed fasciotomies at 4, 8, or 12 h. Animals treated at 4 h demonstrated the return of normal peroneal NCV, irrespective of compartment pressure. When fasciotomies were performed at 12 h, NCV remained poor, suggestive of irreversible injury. They concluded that fasciotomy at 8 h was likely to be sufficient to avoid the irreversible sequelae of compartment syndrome.

Subsequently, Ricci et al. [20] used a canine model of compartment syndrome, which involved vascular isolation at the level of the popliteal artery for 8 h followed by 16 h of monitoring. This technique generated a mean compartment pressure of 112 mm Hg in the untreated control group immediately after reperfusion. A significant reduction in necrosis was identified when fasciotomies were performed immediately before reperfusion, which was lost if the fasciotomy was delayed until 2 h after reperfusion.

In aggregate, there are a number of animal models studying the effect of elevated extremity compartment pressures. The majority use artificial means to generate the requisite pressure, rather than ischemia; follow-up is often limited and outcomes are based on histology rather than functional outcomes. However, there does appear to be broad agreement that a compartment pressure  $>30$  mm Hg is associated with muscle necrosis, which can be limited by early fasciotomy.

The model in the present study overcomes many of these shortcomings by using iliac arterial interruption to deliver an ischemic insult, along with a relatively long follow-up using functional outcome scoring. The iliac artery occlusion with ligation of the lateral circumflex artery rendered the limb ischemic with minimal collateral flow that was confirmed via angiograms in the previous work of this group (unpublished imaging). However, despite this, measured compartment pressures did not consistently exceed 30 mm Hg, even in the 6 h ischemic group. Importantly, this does not permit the evaluation of prophylactic fasciotomy in the setting of insult known to generate compartment syndrome. It may be the case that higher compartment pressures can be generated with longer periods of ischemia, the addition of further injuries (e.g., soft tissue or bony) disruption, or the greater use of crystalloid based resuscitation.

## 5. Conclusions

This study is the first to characterize the effect of porcine extremity ischemia, with concomitant shock, on compartment pressure and functional outcome. An elevation in compartment pressures was observed, although these were below current threshold definitions of compartment syndrome. Following the use of prophylactic fasciotomies, there was no difference in functional outcome measures at 2 wk. This study does not support the use of prophylactic fasciotomies in patients where compartment pressures are not demonstrated to exceed current threshold definitions. Further study is required in a model of compartment syndrome to

further assist in determining the role of prophylactic fasciotomies.

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## Disclosure

The authors reported no proprietary or commercial interest in any product mentioned or concept discussed in the article.

## REFERENCES

- [1] Clouse WD, Rasmussen TE, Peck MA, et al. In-theater management of vascular injury: 2 years of the Balad Vascular Registry. *J Am Coll Surg* 2007;204:625.
- [2] Fox CJ, Gillespie DL, Donnell SD, et al. Contemporary management of wartime vascular trauma. *J Vasc Surg*; 2004:638.
- [3] Stannard A, Brown K, Benson C, et al. Outcome after vascular trauma in a deployed military trauma system. *Br J Surg* 2011; 98:228.
- [4] Gifford SM, Aidinian G, Clouse WD, et al. Effect of temporary shunting on extremity vascular injury: an outcome analysis from the Global War on Terror vascular injury initiative. *J Vasc Surg* 2009;50:549.
- [5] Sohn VY, Arthurs ZM, Herbert GS, Beekley AC, Sebesta JA. Demographics, treatment, and early outcomes in penetrating vascular combat trauma. *Arch Surg* 2008;143:783.
- [6] Borut LTJ, Acosta CJ, Tadlock L, et al. The use of temporary vascular shunts in military extremity wounds: a preliminary outcome analysis with 2-year follow-up. *J Trauma* 2010;69:174.
- [7] Percival TJ, Rasmussen TE. Reperfusion strategies in the management of extremity vascular injury with ischaemia. *Br J Surg* 2012;99:66.
- [8] Tiwari A, Haq AI, Myint F, Hamilton G. Acute compartment syndromes. *Br J Surg* 2002;89:397.
- [9] Percival TJ, White JM, Ricci MA. Compartment syndrome in the setting of vascular injury. *Perspect Vasc Surg Endovasc Ther* 2011;23:119.
- [10] Abouzezzi Z, Nassoura Z, Ivatury RR, Porter JM, Stahl WM. A critical reappraisal of indications for fasciotomy after extremity vascular trauma. *Arch Surg* 1998;133:547.
- [11] Field CK, Senkowsky J, Hollier LH, et al. Fasciotomy in vascular trauma: is it too much, too often? *Am Surg* 1994;60:409.
- [12] Velmahos GC, Theodorou D, Demetriadis D, et al. Complications and nonclosure rates of fasciotomy for trauma and related risk factors. *World J Surg* 1997;2:247.
- [13] Hancock HM, Stannard A, Burkhardt GE, et al. Hemorrhagic shock worsens neuromuscular recovery in a porcine model of hind limb vascular injury and ischemia-reperfusion. *J Vasc Surg* 2011;53:1052.
- [14] Burkhardt GE, Spencer JR, Gifford SM, et al. A large animal survival model (*Sus scrofa*) of extremity ischemia/

reperfusion and neuromuscular outcomes assessment: a pilot study. *J Trauma* 2010;69:S146.

[15] Ritenour AE, Dorlac WC, Fang R, et al. Complications after fasciotomy revision and delayed compartment release in combat patients. *J Trauma* 2008;64:S153.

[16] Sheridan G, Matsen F. An animal model of the compartmental syndrome. *Clin Orthop* 1975;113:36.

[17] Kalns J, Cox J, Baskin J, et al. Threshold model for extremity compartment syndrome in swine. *J Surg Res* 2011;167:e13.

[18] Hargens A, Schmidt D, Evans K. Quantitation of skeletal-muscle necrosis in a model compartment syndrome. *J Bone Joint Surg* 1981;63:631.

[19] Rorabeck C, Clarke K. The pathophysiology of the anterior tibial compartment syndrome: an experimental investigation. *J Trauma* 1978;18:299.

[20] Ricci MA, Corbisiero RM, Mohamed F, Graham AM, Symes JF. Replication of the compartment syndrome in a canine model: experimental evaluation of treatment. *J Invest Surg* 1990;3:129.